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(54) Novel intravenous solutions for influencing renal function and for maintenance therapy.

(57) Disclosed is a novel sterile electrolyte intravenous solution comprising essentially physiological concentrations of sodium and other cations and in general higher than physiological concentrations of bicarbonate. The solution is useful for the treatment of altered renal function and prophylactic treatment of a patient to resist onset of altered renal function.

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NOVEL INTRAVENOUS SOLUTIONS FOR INFLUENCING RENAL FUNCTION AND FOR MAINTENANCE THERAPY

BACKGROUND OF THE INVENTION

This invention relates to novel intravenous solutions for influencing renal function and for follow-up maintenance therapy. An intravenous solution of the invention is more particularly for treating altered renal function or for prophylactically conditioning the kidney to resist that the kidney enters a condition of altered renal function. The term altered renal function as employed herein means a qualitatively and quantitatively depleted or insufficient production of urine, insufficient clearance of metabolic and toxic substances normally cleared by the kidney such as electrolytes, urea, creatinine, phosphates, endogenous and exogenous toxins, pharmaceuticals and their metabolites, a depleted or insufficient ability of the kidney to acidify the urine by excretion of non-volatile or strong acids, or a depleted or insufficient capability of the kidney to produce bicarbonate and thus inability of the kidney to maintain a metabolic acid-base balance within acceptable limits. In such conditions, the therapy normally involves administration of diuretics, preferably loop diuretics, to encourage diuresis.

The intravenous solution of the invention in general finds application in treating patients preliminary to, during and after surgical intervention or any other condition or treatment which may lead to altered renal function. Examples of treatment with potentially nephrotoxic substances include contrast media, antibiotics, cytostatics, cytotoxic drugs, and immuno suppressive drugs. A wide variety of solutions, some being described as substitution fluids are employed for intravenous administration. Commonly used solutions and their compositions are shown in the following Table 1:

TABLE I

Solution	Solute	Concentrations g/100 ml	Ionic concentration mval/litre (Na^+)	(K^+)	(Ca^{2+})	(Cl^-)	(HCO_3^-)
Dextrose in water							
5.00%	Glucose	5.00	...	...	...	...	...
10.00%	Glucose	10.00	...	...	...	...	...
Saline							
Hypotonoc (0.45 %, half normal)	NaCl	0.45	77	-	-	77	-
Isotonic (0.9 %, normal)	NaCl	0.90	154	-	-	154	-
Hypertonic	NaCl	3.00	513	-	-	513	-
		5.00	855	-	-	855	-
Dextrose in saline							
5 % in 0.22 %	Glucose	5.00	-	-	-	-	-
	NaCl	0.22	38.5	-	-	38.5	-
5 % in 0.45 %	Glucose	5.00	-	-	-	-	-
	NaCl	0.45	77	-	-	77	-
5 % in 0.9 %	Glucose	5.00	-	-	-	-	-
	NaCl	0.90	154	-	-	154	-
Ringer's	NaCl	0.86	147	4	5	156	-
	KCl	0.03					
	$CaCl_2$	0.03					
Lactated Ringer's	NaCl	0.60					
	KCl	0.03					
	$CaCl_2$	0.02	130	4	3	109	28
	Na lactate	0.31	0.31				
Hypertonic sodium bicarbonate (0.6 M)	$NaHCO_3$	5.00	595	-	-	-	595
Hypertonic sodium bicarbonate (0.9 M)	$NaHCO_3$	7.50	893	-	-	-	893
Potassium chloride	KCl	14.85	...	211	...	2	

Administration of the Dextrose solutions is physiologically equivalent to the administration of distilled water since glucose is rapidly metabolized to CO_2 and H_2O. The Dextrose is however essential to render the solution isotonic and thus avoid hemolysis. The Saline solutions are most commonly administered since most patients in need of treatment are not only water-depleted but also Na^+ depleted, i.e. salt-depleted.

The plasma Na^+ concentration can be employed to assist in determining which of the above Dextrose, Saline or Dextrose in Saline solutions is most appropriate. The Dextrose solutions provide a small amount of calories, for example the 5 % Dextrose or 5 % Dextrose in 0,22 % saline is equivalent to 200 kcal per litre of solution.

The Ringer's solutions comprised in the above Table include physiologic amounts of K^+ and Ca^{++} in addition to NaCl. The lactated Ringer's solution comprising 28 mEq of lactate per litre (which metabolizes to HCO_3^-) has a composition close to that of extracellular fluid.

The hypertonic Sodium bicarbonate solutions ar primarily employed in the treatment of metabolic acidosis for example by administration of a 7.5 % or higher solution comprised in 50 ml ampuls, but can be added to other intravenous solutions, however not including the Ringer's solutions since precipitation of the HCO_3^- with the Ca^{++} would take place. Similarly, the Potassium Chloride solution can be added to other intravenous solutions, but care needs to be taken not to intravenously administer any concentrated solution of K^+ since this can produce an excessive or too rapid increase in plasma concentration of K^+, which can be fatal.

Other than the above-mentioned hypertonic Sodium bicarbonate solutions, none of the above solutions are known to have any specific influence on kidney function. The hypertonic Sodium bicarbonate solutions on the other hand are normally administered only in limited quantities, at most in quantities sufficient to temporarily correct, normally only in part, a condition of metabolic acidosis. Suggestions to intravenously administer higher quantities of the available Sodium bicarbonate solutions has met with understandable resistance in view particularly of the fact that such solutions are strongly hypertonic and all comprise very much more than or less than physiological amounts of cation solute. Thus, for example the above-mentioned higher concentration 7.5 % Sodium bicarbonate solution available in 50 ml ampuls comprises about 900 mval of Na^+, and 900 mval of HCO_3^- per litre of solution which is neither physiological for Na^+ nor for HCO_3^- . In contrast, the normal value for Na^+ in the blood is from 135 to 146 mval/litre and the normal value for HCO_3^- is 22 to 26 mval/litre.

SUMMARY OF THE INVENTION

In accordance with the invention, it has been found that relatively large quantities of a solution comprising higher than physiological concentrations of HCO_3^- can be intravenously administered provided that the Sodium content of the solution is not significantly different from physiological levels, i.e. not significantly different from about 135 to about 146 mval/litre. Sodium is the most important electrolyte cation and any significant deviation from physiological concentrations as could arise from i.v. administration of any larger quantity of intravenous solution containing more or less than physiological levels of Na^+ may create undesirable and dangerous side effects. Thus, if for example any substantial quantity, say in excess of 200 ml, of the 7.5 % (0.9 M) i.v.sodium bicarbonate solution discussed above were administered to a patient, the patient would tend towards a condition of hypersodemia which has toxic consequences. A condition of hyposodemia similarly can have life endangering consequences so that in general and presuming that the sodium levels in the serum of the patient are within physiological limits, the intravenous solution of the invention comprises a sodium concentration which substantially matches physiological concentrations. On the other hand, as already indicated, the bicarbonate anion concentration in the solution can be very substantially higher than physiological concentrations. However, concentrations of bicarbonate as high as those comprised in known sodium bicarbonate intravenous solutions are not contemplated. The reason is that an excessive or too rapid an increase of bicarbonate in plasma can be fatal as a consequence of systemic alkalosis or hypercapnea (excessive CO_2 concentration arising from decomposition of HCO_3^- into CO_2 and H_2O). Other anions and cations comprised in the intravenous solution of the invention would in general be within or close to physiological levels. Thus, potassium cation would normally be present in the solution at physiological concentrations but could be left away especially if the patient is inclined to hyperkalemia as is sometimes the case. Similarly, chloride anion would be present at physiological levels but can be lower, which latter solution can find use for a patient which is in a condition of hyperchloremic acidosis, as is also sometimes the case.

In the major proportion of cases in which intravenous infusion of fluids is required, the functioning of the kidney of the patient, even if the kidney was initially healthy, may have been or will be altered by a planned medical intervention. For example, renal dysfunction and failure can be a result of heavy injury or massive intervention. Also, however, many patients requiring infusion of fluids, are in any case already suffering from altered or impaired renal function, e.g. because of age or pre-existing disease. Kidney functions are inadequate in a large majority of cases and it is an object of the present invention to provide a novel intravenous solution which is able in particular to acidify the urine, i.e. to increase the capacity of the kidney to excrete hydrogen ions and metabolic acids in the urine, and to increase the volume of urine i.e. the excretion of excess water, (along with increased clearance of substances normally entrained in the urine). Furthermore, in general, the novel solutions of the present invention can serve to correct any systemic acid-base or electrolyte disorders which may be associated with a condition of acute or chronic renal failure or prevention thereof requiring treatment by intravenous infusion of fluids.

The intravenous solutions of the invention essentially act on the whole length of the renal nephron-segm nts, i.e. the renal tubulae, in particular on the proximal tubulae, whereas loop diuretics essentially act

on the distal tubulae. A combination of the two effects enables the action of the loop diuretic to be potentiated which can offer means for reducing the dose required, and diuresis to be increased. The supply of bicarbonate contained in the solutions of the invention provide an essential substrate for beneficial conditioning renal function.

DETAILED DESCRIPTION OF THE INVENTION

An intravenous solution in accordance with the invention comprises at least the following anions and cations, in amounts, i.e. concentrations, within the ranges indicated in the following Table II:

	mval/litre	(preferably)
Na^+	130 to 150	135 to 146
K^+	0 to 6	2 to 5
Cl^-	80 to 125	90 to 110
HCO_3^-	25 to 30 to 70	40 to 60

A typical solution useful for treating altered renal function comprises the following amounts and concentrations of electrolytes:

		mval/litre	
Sodium Chloride	5.026 g	Na^+	146
Potassium Chloride	0.298 g	K^+	4
Sodium Bicarbonate	5.040 g	Cl^-	90
Water for infusion solution to	1000.0 ml	HCO_3^-	60

Once treatment with a solution such as above has achieved the desired results for a reasonable period, i.e. increased urine volume and stabilized acid-base balance for 24 hours or more, a solution comprising less bicarbonate ions, i.e. less than 40 mval/litre but not lower than physiological levels, i.e. 25 mval/litre may be employed for maintenance therapy. However, since it is important that sodium levels not depart significantly from physiological levels, lowering of the bicarbonate content requires an increase in Sodium Chloride content which in turn leads to an increase in Chloride content. Hyperchloremia is often attendent to altered renal function so that increased chloride above physiological levels would in general be avoided.

The dose of intravenous solution administered will of course depend on the weight of the patient, the condition of the patient, specifically the fluid balance, and the effect desired. However, in general, satisfactory results for treating altered renal function and achievement of increased urine volume and associated desired results such as increased clearance of metabolites and toxins, fixed or strong acids, phosphates and the like are obtained when a solution comprising more than about 40 mval/litre of bicarbonate anion is administered at a rate of from 50 to 500 ml of solution/hour (about 15 to 180 drops/min). The total dose required for an adult in twenty-four hours can be as much as 12 litres (= 500 ml/hour). An indication of whether or not the dose is adequate can be obtained by blood gas analysis and by measuring fresh urine pH value. If the urine pH value tends towards or is slightly greater than 7.0, adequate dosage has been achieved. Exemplary clinical trials performed with a bicarbonate-electrolyte solution of the invention are summarized below. The six patients were all urological post-operative patients suffering from prostate or kidney carcinoma.

Diagnosis: Prostate-Carcinoma
Operation: Radical Lymphadenectomy
Progression: Diuresis:
1st day: 1085 ml
2nd day: 4130 ml

3rd day: 5270 ml
4th day: 4600 ml
5th day: 1550 ml up to 6 p.m.
(otherwise from 6 a.m. to 6 a.m.)
Infusion program:

1st day:	3000 ml Bicarbonate-electrolyte solution
	1000 ml Glucose 5 %
2nd day:	2000 ml Combiplasmal
	2000 ml Bicarbonate-electrolyte solution + 20 mg Lasix + 40 mval KCl
	1000 ml Ringer
3rd day:	2000 ml Bicarbonate-electrolyte solution + 20 mg Lasix + 40 mval KCl
	2000 ml Combiplasmal
	500 ml Glucose 5 %
	1000 ml Ringer
4th day:	2000 ml Bicarbonate-electrolyte solution + 20 mg Lasix + 40 mval KCl
	1000 ml Glucose 5 %
	160 ml Combiplasmal
	1000 ml Aminosteril 10 %
	2000 ml Ringer
5th day:	500 ml Aminosteril 10 %
	500 ml Glucose 5 %
	1000 ml Ringer
	1000 ml Bicarbonate-electrolyte solution + 20 mg Lasix + 20 mval KCl infused up to 6 p.m.

Balance:	1st day:	2715 ml
	2nd day:	870 ml
	3rd day:	680 ml
	4th day:	1310 ml
	5th day:	no balance established

Serum values:

1st day:	pH 7,37, PCO_2 39 mmHg, HCO_3^- 23 mmol/l, BA - 1.6.
2nd day:	pH 7,42, PCO_2 42 mmHg, HCO_3^- 28 mmol/l, BA + 3.6.
	Urea-N. 27 mg/dl (7-18), Creatinine 2,3 mg/dl, Ca 8,4 mg/dl
	Phosphorous (inorg) 5,5 mg/dl, Protein 5,2 g/dl (other values normal)
3rd day:	all values normal except Urea-N. 26 mg/dl, Creatinine 2,0 mg/dl Uric acid 8,3 mg/dl, K^+ 3,2 mmol/l.
4th day:	all values normal except Urea-N. 25 mg/dl, Creatinine 1,6 mg/dl
	K^+ 3,3 mmol/l, Protein 5,6 g/dl.
5th day:	pH 7,41, PCO_2 46 mmHg, HCO_3^- 29 mmol/l, BA + 4,2.
	Urea-N. 33 mg/dl, Creatinine 1,5, mg/dl, K^+ 3,4 mmol/l,
	Ca 8,5 mg/dl, Protein 5,9 g/dl.

Normal range of Serum values:
Blood gas analysis, venous blood:

pH	7,32 - 7,38
PCO_2	42 - 50 mmHg
HCO_3^-	23 - 27 mmol/l
BA	0 ± 2,3 mmol/l (BA = base excess / or deficit value)

Serum values:

Urea-N	7 - 18 mg/dl
Creatinine	0,5 - 1,3 mg/dl
Uric acid	3 - 7 mg/dl
Phosphorous (inorg)	2,5 - 4,5 mg/dl
Protein	6,0 - 8,0 g/dl
Na^+	135 - 146 mmol/l
K^+	3,5 - 5,0 mmol/l
Cl^-	97 - 108 mmol/l
Calcium (total)	8,7 - 10,5 mg/dl

Summary:
High daily urine volumes, uncomplicated progression. Transferred to General clinic on 5th postoperative day. Adequate control of serum metabolites concentration. Electrolyte and acid-basis-balance essentially normal, mild potassium- and Protein-deficit. Observation period 5 days.
Diagnosis: Kidney-Carcinoma
Operation: Nephrectomy
Progression: Diuresis:
1st day: 2280 ml
2nd day: 2020 ml
3rd day: 1700 ml (intensive transpiration)
4th day: 2640 ml
Infusion program:

1st day:	2000 ml Bicarbonate-electrolyte solution + 20 mg Lasix + 40 mval KCl
	1000 ml Glucose 5 %
2nd day:	1000 ml Glucose 5 %
	2000 ml Bicarbonate-electrolyte solution + 40 mval KCl + 20 mg Lasix
3rd day:	2000 ml Bicarbonate-electrolyte solution + 40 mval KCl + 20 mg Lasix
	1000 ml Glucose 5 %
	500 ml Ringer
4th day:	2000 ml Bicarbonate-electrolyte solution + 20 mg Lasix + 40 mval KCl
	1000 ml Glucose 5 %
5th day:	2000 ml Bicarbonate-electrolyte solution + 20 mg Lasix + 40 mval KCl
	1000 ml Glucose 5 %
6th day:	1000 ml Bicarbonate-electrolyte solution
	500 ml Glucose 5 %

Balance:	1st day:	+ 570 ml
	2nd day:	+ 1530 ml
	3rd day:	+ 1600 ml
	4th day:	+ 1000 ml
	5th day:	+ 1300 ml

Serum values:

1st day:	not determinated
2nd day:	Uriea-N 19 mg/dl, Creatinine 1,8 mg/dl, Ca 7,8 mg/dl, Protein 5,4 g/dl, (other values normal). pH 7,45, PCO_2 45 mmHg, HCO_3^- 31 mmol/l, BA + 7,1.
3rd day:	Urea-N 34 mg/dl, Creatinine 2,5 mg/dl, Uric-acid 7,6 mg/dl Ca 8,1 mg/dl, Protein 5,6 g/dl, (other values normal) pH 7,49, PCO_2 40 mmHg, HCO_3^- 30 mmol/l, BA + 7,1.
4th day:	Urea-N 49 mg/dl, Creatinine 2,4 mg/dl, Ca 7,4 mg/dl, Protein 5,2 g/dl, (other values normal)
5th day:	pH 7,46, PCO_2 33 mmHg, HCO_3^- 23 mmol/l, BA + 1,1. Urea-N 46 mg/dl, Creatinine 2,0 mg/dl, Protein 5,6 g/dl, Ca 8,0 mg/dl, (other values normal)
6th day:	Urea-N 37 mg/dl, Creatinine 1,9 mg/dl, Ca 8,2 mg/dl.

Summary:

High daily urine volumes. The observation period ended on the 6th day, when the patient was transferred to the General clinic. In general satisfactory progress. Essentially stabilized acid/base status, including serum concentration of metabolites, electrolytes. Na, K, Cl always at normal levels.
Diagnosis: Prostata-Carcinoma
Operation: Radical Prostatectomy, Pelvine Lymphadenectomy
Progression: Diuresis:

1st day:	1380 ml
2nd day:	4400 ml
3rd day:	4100 ml
4th day:	4250 ml
5th day:	4450 ml
6th day:	4100 ml

Infusion program:

1st day:	1000 ml Bicarbonate-electrolyte solution
(after 3 p.m.)	1000 ml Glucose 5 %
	1000 ml Ringer
2nd day:	2000 ml Combiplasmal
	500 ml Lipofundin
	500 ml Glucose 5 %
	2000 ml Bicarbonate-electrolyte solution + 20 mg Lasix + 40 mval KCl
	500 ml Glucose 5 %
3rd day:	2000 ml Bicarbonate-electrolyte solution
	2000 ml Combiplasmal
	1000 ml Glucose 5 %
	500 ml Lipofundin
4th day:	500 ml Lipofundin
	2000 ml Combiplasmal + 20 mval KCl
	2000 ml Bicarbonate-electrolyte solution + 20 mg Lasix + 40 mval KCl
	100 ml Humanalbumin
5th day:	500 ml Lipofundin
	2000 ml Bicarbonate-electrolyte solution + 20 mg Lasix + 40 mval KCl
	2000 ml Combiplasmal + 20 mval KCl
	500 ml Glucose 5 %
	1000 ml Ringer
6th day:	500 ml Lipofundin
	1000 ml Combiplasmal
	2000 ml Bicarbonate-electrolyte solution + 20 mg Lasix + 40 mval KCl
	500 ml Glucose 5 %

7th day: 500 ml Lipofundin
500 ml Glucose 5 %
1000 ml Combiplasmal
1000 ml Bicarbonate-electrolyte solution + 20 mg Lasix + 20 mval KCl
all drugs until 12 a.m. then transferred

Balance:
1st day: + 1670 ml
2nd day: + 350 ml
3rd day: + 1550 ml
4th day: + 1120 ml
5th day: + 2280 ml
6th day: + 750 ml

Serum values:

1st day: pH 7,36, PCO_2 48 mmHg, HCO_3^- 27 mmol/l, BA + 1.5.
2nd day: Protein 4,9 g/dl (6-8), Ca 7,6 mg/dl (8,7-10,5), other values normal.
pH 7,41, PCO_2 39 mmHg, HCO_3^- 25 mmol/l, BA + 1,3.
3rd day: Potassium 3,4 mmol/l, Protein 4,9 g/dl (6-8),
pH 7,41, PCO_2 48 mmHg, HCO_3^- 31 mmol/l, BA + 5,6.
4th day: Potassium 3,3 mmol/l, Ca 7,8 mg/dl, Protein 4,7 g/dl,
pH 7,43, PCO_2 39 mmHg, HCO_3^- 27 mmol/l, BA + 3,1.
5th day: Potassium 3,5 mmol/l, Ca 8,2 mg/dl, Protein 5,3 g/dl,
pH 7,42, PCO_2 42 mmHg, HCO_3^- 27 mmol/l, BA + 2,5.
6th day: Ca 8,0 mg/dl (8,7-10,5), Protein 5,1 g/dl,
pH 7,42, PCO_2 42 mmHg, HCO_3^- 27 mmol/l, BA + 2,6.
7th day: Ca 8,1 mg/dl, Protein 5,1 g/dl,
pH 7,42, PCO_2 41 mmHg, HCO_3^- 27 mmol/l, BA + 2,6.

Summary:
Very high daily urine volumes. Uncomplicated progression, stabilized metabolites, electrolytes and acid-basis-balance, mild potassium-, calcium- and protein-deficit. Transferred to General clinic on 7th postoperative day.
Diagnosis: Kidney-Carcinoma
Operation: Nephrectomy
Progression: Diuresis:

1st day: 2760 ml
2nd day: 620 ml up to 10 a.m.

Infusiun program:

1st day:	1000 ml Bicarbonate-electrolyte solution
	2000 ml Bicarbonate-electrolyte solution + 20 mg Lasix + 40 mval KCl
	500 ml Glucose 5 %
	500 ml Ringer
2nd day:	1000 ml Combiplasmal
	1000 ml Bicarbonate-electrolyte solution + 20 mval KCl + 10 mg Lasix
	250 ml Glucose 50 %, up to 10 a.m.

Balance:	1st day:	+ 1240 ml
	2nd day:	not evaluated

Serium values:

1st day:	normal
2nd day:	Protein 4,9 g/dl, Creatinine mg/dl 1,4 mg/dl, Calcium 7,8 mg/dl, pH 7,44, PCO_2 45 mmHg, HCO_3^- 30 mmol/l, BA + 6.

Summary:
High daily urine volumes. Uncomplicated progression. Transferred to General clinic on 2nd postoperative day. Stabilized metabolites electrolytes and acid-basis balance. Mild protein- and Ca-deficit.
Diagnosis: Kidney-Carcinoma
Operation: Ventral Nephrectomy with Lymphadenectom
Progression: Diuresis:

1st day:	2800 ml
2nd day:	2700 ml

Infusion program:

1st day:	1000 ml Ringer (OP)
	2000 ml Bicarbonate-electrolyte solution + 20 mg Lasix + 40 mval KCl
2nd day:	2000 ml Combiplasmal
	2000 ml Bicarbonate-electrolyte solution + 20 mg Lasix + 40 mval KCl
	500 ml Glucose 5 %

Balance:	1st day:	+ 200 ml
	2nd day:	+ 1700 ml

Serum values:

. 1st day: not evaluated

2nd day: normal except Creatinine mg/dl 2,0 mg/dl

pH 7,43, PCO_2 42 mmHg, HCO_3^- 28 mmol/l, BA + 3,9.

Summary:
High daily urine volumes. Progression without complications. Observation period 2 days. Metabolites concentration, electrolytes and blood gases essentially normal.
Diagnosis: Stenosis of Urethra, Prostata-Carcinoma, Diab. mellitus
Operation: Pelvine Lymphadenectomy
Progression: Diuresis:

1st day:	2880 ml
2nd day:	2200 ml
3rd day:	4030 ml

Infusion program:

1st day:	2000 ml Bicarbonate-electrolyte solution, + 20 mg Lasix + 40 mval KCl
	1000 ml Glucose 5 %
2nd day:	2000 ml Bicarbonate-electrolyte solution, 40 mval KCl, 20 mg Lasix
	1000 ml Glucose 5 %
3rd day:	2000 ml Bicarbonate-electrolyte solution, + 40 mval KCl, 20 mg Lasix
4th day:	1000 ml Bicarbonate-electrolyte solution, + 40 mval KCl, 20 mg Lasix
Balance:	1st day: - 470 ml
	2nd day: + 1490 ml
	3rd day: - 530 ml

Serum values:

1st day:	Urea-N. 21 mg/dl (norm 7-18), Uric acid 8,9 mg/dl (-7)
	other values normal
2nd day:	mild higher value of Urea N. and Uric acid
	Protein 4,9 g/dl (6-8), Ca 7,8 mg/dl (8,7-10,5)
	pH 7,41, PCO_2 49 mmHg, HCO_3^- 31 mmol/l, BA + 5,4
3rd day:	Chloride 96 mmol/l (97-108), Ca. 7,8 mg/dl, Protein 4,9 g/dl
	other values normal
	pH 7,49, PCO_2 48 mmHg, HCO_3^- 37, BA + 12,5
4th day:	Uric acid. 8,9 mg/dl, Potassium 3,4 mmol/l, Ca 8 mg/dl
	Phospor 2,3 mg/dl (2,5-4,5), Protein 4,9 g/dl
	other values normal

Summary:
High daily urine volumes. Stabilized metabolites, electrolytes-valu s, Protein mildly lower. Transferred to General clinic on 4th postoperativ day = end of observation. Uncomplicated progression.

Of course, the solutions of the invention may comprise additional substances, such as pharmaceuticals,

trace elements, soluble and stabl Ca and/or Mg compounds. The components of the solutions may be provided in combined or separated form. For xample Ca and/or Mg compounds or components may be provided in a container, such as a flexible bag, separate from the bicarbonate component.

Claims

1. A sterile intravenous solution comprising at least the following electrolytes at the concentrations indicated:

	mval/litre
Na^+	130 to 150
K^+	2 to 5
Cl^-	80 to 125
HCO_3^-	25 to 30

2. A sterile intravenous solution according to claim 1, comprising the electrolytes at the following concentrations:

	mval/litre
Na^+	135 to 146
K^+	2 to 5
Cl^-	90 to 110
HCO_3^-	40 to 60

3. A sterile intravenous solution according to claim 1 or claim 2, which is provided in conjunction with a sterile solution of a Ca and/or Mg compound.

4. A sterile intravenous solution according to claim 3, in which the sterile solution of the Ca and/or Mg compound is provided in a container, such as a flexible bag, which is separate from the HCO_3^- electrolyte.

European Patent Office

EUROPEAN SEARCH REPORT

Application Number

EP 91 10 0527

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.5)
X	WO-A-8 703 808 (RICHARD L. VEECH) * the whole document *	1-3	A 61 K 33/14 A 61 K 33/10 A 61 M 1/16
X	WO-A-8 703 809 (RICHARD L. VEECH) * the whole document *	1,3	
X	EP-A-0 177 614 (TOMITA PHARMACEUTICAL CORPORATION LIMITED) * the whole document *	1-3	
A	DE-A-2 358 759 (CYBERSOL INC.) * the whole document *	1-4	
A	EP-A-0 076 658 (ALCON LABORATORIES INC.) * the whole document *	1-4	

TECHNICAL FIELDS SEARCHED (Int. Cl.5)

A 61 K
A 61 M

The present search report has been drawn up for all claims

Place of search	Date of completion of search	Examiner
Berlin	08 May 91	SIATOU E

CATEGORY OF CITED DOCUMENTS

X: particularly relevant if taken alone
Y: particularly relevant if combined with another document of the same catagory
A: technological background
O: non-written disclosure
P: intermediate document
T: theory or principle underlying the invention

E: earlier patent document, but published on, or after the filing date
D: document cited in the application
L: document cited for other reasons

&: member of the same patent family, corresponding document